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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
BABIC, CHRISTOPHER M	
ART UNIT	**PAPER NUMBER**
1637	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/666,806	AYDIN, ATAKAN	
	Examiner	Art Unit	
	Christopher M. Babic	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 April 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4 and 5* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 2,4,5* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on April 18, 2007 has been entered. Claim(s) 1, 2, 4, and 5 are pending.

Claim Rejections - 35 USC § 102

The rejections of claim(s) 1-10 over Schouten as set forth in the Office Action dated April 18, 2007 have been withdrawn in view of Applicant's amendments.

Response to Arguments

Applicant's arguments have been fully considered but they are moot in view of the new grounds of rejection presented below.

New Grounds of Claim Rejections - 35 USC § 103

The rejections of claim(s) 1-10 over Barany in view of Wittwer and Godfrey as set forth in the Office Action dated April 18, 2007 have been withdrawn in view of Applicant's amendments.

The following new grounds of rejections are made in view of Applicant's amendments.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim(s) 1, 2, 4, and 5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schouten (EP 1 130 113 A1; 5 September 2001) in view of Sorge (U.S. 6,350,580 B1).

With regard to claim(s) 1, Schouten teaches methods for detecting the at least one target nucleic acid sequence in a sample (fig. 2,3; pg. 11-18, for example) comprising a method for detecting at least one target nucleic acid sequence in a sample comprising" forming a ligation reaction composition comprising the sample and a ligation probe set for each target nucleic acid sequence, the probe set comprising (a) at least one first probe, comprising a target-specific portion and a 5' primer-specific portion, wherein the 5' primer-specific portion comprises a sequence, and (b) at least one second probe, comprising a target-specific portion and a 3' primer-specific portion, wherein the 3' primer-specific portion comprises a sequence, wherein the probes in each set are suitable for ligation together when hybridized adjacent to one another on a complementary target nucleic acid sequence.

With regard to the phrase, "...and wherein one probe in each probe set further comprises an addressable portion located between the primer-specific portion and the target-specific portion, wherein the addressable portion comprises a sequence," and subsequent claim limitations, the disclosure of Schouten expressly teaches a --stuffer sequence-- (pg. 11, lines 40-55; pg. 14, lines 25-45, for example), located between primer-specific portion and the target-specific portion of a probe (pg. 11, 50-55, for example), can contain a sequence that can be used to discriminate by the use of fluorogenic probes and the 5' nuclease activity of some polymerases (i.e. real time detection) (pg. 14, lines 25-45, for example). Thus, if a particular probe set failed to ligate due to a particular nucleotide mismatch (i.e. SNP or allele), it would fail to produce a threshold value in subsequent amplification reactions (and vice versa) thereby allowing one to determine a particular allele at a given locus (i.e. heterozygosity or homozygosity) by comparison of threshold values.

Schouten does not expressly teach the use of a labeled probe for use in a FEN nuclease based detection assay.

With regard to the above claim(s) as well as claim(s) 2, 4, and 5, Sorge provides a supporting disclosure that teaches a method of monitoring amplification reactions (middle-end col. 18; middle-end col. 53, for example) through the use of a FEN nuclease (col. 23-29, for example) and probes (col. 36-39, for example) that comprise interactive FRET labels (end col. 44, for example) and a 5' cleavage structure (middle col. 4, for example).

As Sorge highlights, their invention answered a need in the art for amplification product detection methods, both concurrent and post-amplification, that did not require multiple cumbersome steps (end col. 3-4, for example).

Thus, in summary, it is submitted that it would have been *prima facie obvious* to a practitioner of ordinary skill in the art at the time of invention to incorporate the labeled flap endonuclease probe for use in the detection assays of Sorge within the amplification methods of Schouten since Sorge suggests such a modification to allow for concurrent and post-amplification detection procedures that do not require multiple cumbersome steps.

2. Claim(s) 1, 2, 4, and 5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Barany et al. (U.S. 6,027,889) in view of Wittwer et al. (U.S. 6,303,305), in further view of Godfrey et al. "Quantitative mRNA Expression Analysis from Formalin-Fixed, Paraffin-Embedded Tissues Using 5' Nuclease Transcription-Polymerase Chain Reaction" Journal of Molecular Diagnostics. 2000. Vol. 2, No. 2: Pages 84-91), in further view of Sorge (U.S. 6,350,580 B1).

With regard to claim(s) 1, Barany teaches a method (fig. 8-12; col. 9-11; col. 23-30; col. 41, ex. 4, for example) comprising: forming a ligation reaction composition comprising the sample, and a ligation probe set for each target nucleic acid sequence, the probe set comprising (a) at least one first probe, comprising a target-specific portion and a 5' primer-specific portion, wherein the 5' primer-specific portion comprises a

sequence, and (b) at least one second probe, comprising a target-specific portion and a 3' primer-specific portion, wherein the 3' primer-specific portion comprises a sequence, wherein the probes in each set are suitable for ligation together when hybridized adjacent to one another on a complementary target sequence; forming a test composition by subjecting the ligation reaction composition to at least one cycle of ligation, wherein adjacently hybridizing complementary probes are ligated to one another to form a ligation product comprising the 5' primer-specific portion, the target-specific portions, and the 3' primer-specific portion (fig. 8-12; col. 9-11; col. 23-30; col. 41, ex. 4, for example).

Neither Barany, Wittwer, nor Godfrey expressly teach the use of a labeled probe for use in a FEN nuclease based detection assay.

With regard to the above claim(s) as well as claim(s) 2, 4, and 5, Sorge provides a supporting disclosure that teaches a method of monitoring amplification reactions (middle-end col. 18; middle-end col. 53, for example) through the use of a FEN nuclease (col. 23-29, for example) and probes (col. 36-39, for example) that comprise interactive FRET labels (end col. 44, for example) and a 5' cleavage structure (middle col. 4, for example).

As Sorge highlights, their invention answered a need in the art for amplification product detection methods, both concurrent and post-amplification, that did not require multiple cumbersome steps (end col. 3-4, for example).

Thus, in summary, it is submitted that it would have been *prima facie obvious* to a practitioner of ordinary skill in the art at the time of invention to incorporate the labeled

flap endonuclease probe for use in the detection assays of Sorge within the amplification methods of Schouten since Sorge suggests such a modification to allow for concurrent and post-amplification detection procedures that do not require multiple cumbersome steps.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

It is noted that only representative claims will be discussed in the following rejection(s).

1. Claim(s) 4 is rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim(s) 4 of U.S. Patent No. 7,153,658 B2 in view of Sorge (U.S. 6,350,580 B1).

Although the conflicting claims are not identical, they are not patentably distinct from each other because they are both drawn to the same general inventive concept of detecting a target nucleic acid comprising a real-time ligation detection reaction utilizing a probe comprising a quencher moiety and a fluorescent moiety. The only significant difference between the conflicting claim(s) is the requirement of a flap endonuclease (FEN) by claim 4 of the instant invention.

As set forth above, Sorge provides a supporting disclosure that teaches a method of monitoring amplification reactions (middle-end col. 18; middle-end col. 53, for example) through the use of a FEN nuclease (col. 23-29, for example) and probes (col. 36-39, for example) that comprise interactive FRET labels (end col. 44, for example) and a 5' cleavage structure (middle col. 4, for example).

As Sorge highlights, their invention answered a need in the art for amplification product detection methods, both concurrent and post-amplification, that did not require multiple cumbersome steps (end col. 3-4, for example).

Thus, in summary, it is submitted that it would have been *prima facie obvious* to a practitioner of ordinary skill in the art at the time of invention to incorporate the labeled flap endonuclease probe for use in the detection assays of Sorge within the amplification methods of Schouten since Sorge suggests such a modification to allow

for concurrent and post-amplification detection procedures that do not require multiple cumbersome steps.

2. Claim(s) 1 is provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim(s) 1 of U.S. copending Application No. 10/693609 in view of Sorge (U.S. 6,350,580 B1).

Although the conflicting claims are not identical, they are not patentably distinct from each other because they are both drawn to the same general inventive concept of detecting a target nucleic acid comprising a real-time ligation detection reaction utilizing a probe comprising a quencher moiety and a fluorescent moiety. The instant invention requires that use of a species of amplification product detection, i.e. FEN nuclease probe assay.

As set forth above, Sorge provides a supporting disclosure that teaches a method of monitoring amplification reactions (middle-end col. 18; middle-end col. 53, for example) through the use of a FEN nuclease (col. 23-29, for example) and probes (col. 36-39, for example) that comprise interactive FRET labels (end col. 44, for example) and a 5' cleavage structure (middle col. 4, for example).

As Sorge highlights, their invention answered a need in the art for amplification product detection methods, both concurrent and post-amplification, that did not require multiple cumbersome steps (end col. 3-4, for example).

Thus, in summary, it is submitted that it would have been *prima facie obvious* to a practitioner of ordinary skill in the art at the time of invention to incorporate the labeled flap endonuclease probe for use in the detection assays of Sorge within the amplification methods of Schouten since Sorge suggests such a modification to allow for concurrent and post-amplification detection procedures that do not require multiple cumbersome steps.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

Claim(s) 1, 2, 4, and 5 are rejected. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher M. Babic whose telephone number is 571-272-8507. The examiner can normally be reached on Monday-Friday 7:00AM to 4:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

7/7/7

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